Remarks

The claimed invention

The present claims, which are drawn to methods of treating a subject in need of treatment for malaria, replace previous claims drawn to compositions useful in practicing the methods. The shift to a different claimed invention was discussed in a phone interview between the undersigned and the examiner, conducted on April 12, 2005. Applicant thanks the examiner for exercising his discretion in permitting the shift, in accordance with *Ex parte Heritage*, Pat. No. 2,375,414 decided January 26, 1944 and *Meden v. Curtis*, 1905 C.D.272, 117 O.G. 1795 (Comm'r Pat. 1905) and as set forth in MPEP §819.01.

New claims

New claim 51 is drawn to a method of treating a subject in need of treatment for malaria, wherein the subject is infected with a malaria parasite, the method comprising the step of: administering an antimalarial composition comprising a compound that is an inhibitor of fatty acid synthesis in the malaria parasite to the subject. New claim 52 recites that the inhibitor of fatty acid synthesis is a hydroxydiphenyl ether. New claim 53 describes the structure of certain compounds falling within the scope of claim 52. New claim 54 specifies that the compound is triclosan. New claim 57 recites that the composition is administered by injection. New claim 58 recites that the amount of the inhibitor of fatty acid synthesis administered is in the dosage range of 0.03 mg/kg to 100 mg/kg. New claim 59 recites that the compound inhibits FabI (enoyl ACP reductase). Support for these claims is found throughout the specification, e.g., at p. 10, lines 17-34, at p. 21, lines 6-14, and in original claims 7, 8, 9, 10, 15, 25-29, and 33, among others.. It is noted that the phrase "antimalarial composition" as used in certain of the original claims indicates that the compositions are useful in a method of treating malaria.

New claims 55 and 60 recite that the composition used for treating malaria further further comprises one or more known antimalarial agents and a pharmaceutically acceptable adjuvant, diluent, or carrier. Support is found in original claims 8 and 27. New claims 56 and 61 recite particular known antimalarials. Support is found in the specification, e.g., at p. 2, line 20 – p. 9, line 28. See, e.g., p. 2, line 21.

New claim 62 recites that the inhibitor of fatty acid synthesis in the malaria parasite is an inhibitor of FabI (enoyl-ACP reductase). Support is found in original claim 32.

New claim 63 recites that the malaria parasite is *P. falciparum*. Support is found in original claims 19 and 33 and throughout the specification, e.g., in Example 1 (p. 22).

Title

The Examiner suggested that Applicant may wish to change the word "Glass" to "Class" in the Title. Applicant thanks the Examiner for pointing out that the Patent Office considers the Title to include the word "Glass" instead of "Class". The application was filed with the word "Class" in the Title provided on the Specification and on the Transmittal, but an error was apparently made in entering the Title into the PTO records. A corrected filing receipt has been requested in a petition filed on Jan. 19, 2005.

Rejections under 35 U.S.C. § 112

Claims 7, 9-13, and 36-42 stand rejected under 35 U.S.C. § 112 on the ground that the specification, while being enabling for triclosan, does not reasonably provide enablement for other inhibitors of fatty acid synthesis, such as other hydroxydiphenyl ethers of general formula 2 wherein the X is S and CH_2. Claims 7, 9-13, and 36-42 have been canceled, thereby rendering the rejection moot. Present claim 53 is drawn to methods of treating malaria by administering compounds of formula 2, wherein X is limited to O.

Applicant notes the Examiner's statement that the prior art, Surolia et al., "Triclosan offers protection against blood stages of malaria by inhibiting enoyl-ACP reductase of *Plasmodium falciparum*", "shows only triclosan possesses antimalarial activity". Applicant respectfully submits that the article also discloses that another member of the class of hydroxydiphenyl ethers showed activity. See p. 167, right column, stating, "We found another member of this class of compounds, 2,2' dihydroxydiphenyl ether, to be 0.1% as effective an inhibitor of the *in vitro* growth of *P. falciparum*..." While this compound may be less preferred than triclosan, the results nevertheless show that other compounds in the same class do possess anti-malarial activity. Subsequent studies have demonstrated that additional compounds in this class, in which X = O, also possess activity. Applicant further notes that Model teaches that a number of compounds in this class are useful as antibacterial agents. It would therefore be reasonable to assume that these compounds have at least some biological activities in common.

Claim 42 stands rejected for indefiniteness. Since the claim has been canceled, this rejection is now moot.

Rejections under 35 U.S.C. § 103

Claims 8, 9, and 42-49 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dick or Model in view of Windholz. Claims 8, 9, and 42-49 have been canceled, thereby rendering the rejection moot. However, to the extent that the Examiner may consider applying these references to the currently pending claims, Applicant submits the following remarks regarding the Examiner's rationale for rejecting claims 8, 9, and 42-49.

The Examiner points to Dick, col. 3, lines 36-41, which teaches that a particular inhibitor of Type I fatty acid synthase, cerulenin, is effective against bacteria and protozoa. The Examiner states that "One skilled in the art would have assumed that the combination of a fatty acid synthesis inhibitor, such as cerulenin with chloroquine into a single composition would give an additive effect since cerulenin is effective against protozoa and chloroquine is effective against malaria (caused by a protozoa) in the absence of evidence to the contrary." Applicant submits that Dick only provides evidence for the efficacy of cerulenin against a single protozoa, namely *Toxoplasma gondii*. Dick does not provide or describe any data indicating that cerulenin would be active against other protozoa, e.g., malaria parasites. Protozoa encompass a wide range of different organisms with diverse life cycles and biological features. The Examiner has not provided any evidence to suggest that one of ordinary skill in the art would assume that a compound effective against one particular protozoa would also be effective against other protozoa. Applicant submits that, on the contrary, the fact that a compound is effective against a particular protozoa would not suggest to one of ordinary skill in the art that the compound would also be generally effective against other protozoa. In particular, the fact that a compound is effective against one *T. gondii* would not suggest to one of ordinary skill in the art that the compound would also be effective against malaria parasites. Examples abound of compounds that are useful for treating a particular protozoa but that are not therapeutically useful against malaria parasites. Applicant further submits that Dick teaches that cerulenin is an inhibitor of Type I fatty acid synthase. However, hydroxydiphenyl ethers, as recited in the current claims, are inhibitors of FabI, which is a component of Type II fatty acid synthases.

The Examiner further states that, "one skilled in the art would have assumed the antibacterial properties would be effective against any microorganisms that are harmful to the infected host, thus the properties (antibacterial activity) would be effective against protozoa (a microorganism) absent evidence to the contrary." Applicant respectfully disagrees and submits that the Examiner has not provided any evidence in support of this assumption. The fact that a compound is effective against bacteria would not suggest to one of ordinary skill in the art that the compound would also be effective against protozoa, particularly malaria parasites, simply because both bacteria and protozoa may be considered microorganisms. In fact, the great majority of antibacterial agents are not therapeutically effective against malaria parasites.

Applicant further notes that hydroxydiphenyl ether compounds such as triclosan have heretofore found commercial use externally, e.g., as components in acne creams, toothpastes, soaps, and mouthwashes, or as disinfectants for household goods and other products, rather than internally, as in the treatment or prevention of malaria. See, e.g., Exhibit A, p. 170 (right column), submitted with the Office Action Response filed Feb. 23, 2004. The Examiner has not identified any prior art that teaches or suggests the use of such compounds for purposes of treating or preventing a systemic protozoal infection such as malaria. Applicant, on the other hand, has provided both the motivation to employ this class of compounds for treatment and prevention of malaria and has provided evidence of efficacy both *in vitro* and *in vivo*.

Applicant thanks the Examiner again for his willingness to permit the shift in claim group and for his careful consideration of the present case. In view of the amendments and remarks presented herein, Applicants respectfully submit that the case is in condition for allowance. A Notice to that effect is earnestly requested.

If, at any time, it appears that a phone discussion would be helpful, the undersigned would greatly appreciate the opportunity to discuss such issues at the Examiner's convenience. The undersigned can be contacted at (617) 248-5000 or (617) 248-5071 (direct dial).

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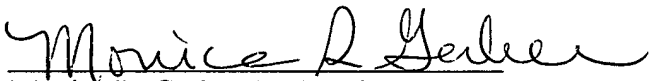
Respectfully submitted,



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